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10/699,502	10/31/2003	Jiong Wu	SRCK:066 12642.0066.NPUS0	3578

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HOWREY LLP
C/O IP DOCKETING DEPARTMENT
2941 FAIRVIEW PARK DRIVE, SUITE 200
FALLS CHURCH, VA 22042-7195

EXAMINER	
HANLEY, SUSAN MARIE	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 06/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/699,502	WU ET AL.	
	Examiner	Art Unit	
	Susan Hanley	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☒ Claim(s) *2,10 and 16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of the following species:

a. an acid selected from formic acid, acetic acid and mixtures thereof of which the system is substantially free; and

b. heat-treated saponins

in the reply filed on 4/19/06 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-19 are presented for examination.

Specification

The abstract of the disclosure is objected to because it is too long. The abstract in an application filed under 35 U.S.C. 111 may not exceed 150 words in length. The purpose of the abstract is to enable the United States Patent and Trademark Office and the public generally to determine quickly from a cursory inspection the nature and gist of the technical disclosure. Correction is required. See MPEP § 608.01(b).

The specification is objected to because it lacks a separate heading and section for the "BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S)". Correction is required. See MPEP 608.01(f).

Claim Objections

Claims 2, 10 and 16 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in

independent form. Claims 2, 10 and 16 are drawn to a composition that further comprises a surfactant. The addition of a surfactant is not further limiting because a saponin is a surfactant.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5, 6-8, 13 and 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a reagent system comprising a saponin, an acid selected from phosphoric acid or a halogenated acid and a quenching agent, and a method of use thereof, wherein the saponin is kept at room temperature or is heated at 121 degrees C, with or without acid, does not reasonably provide enablement for a reagent system comprising a saponin, an acid selected from phosphoric acid or a halogenated acid and a quenching agent, and a method of use thereof, wherein the saponin is heated to any possible temperature, with or without acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claims are drawn to a reagent system comprising a saponin, an acid selected from phosphoric acid or a halogenated acid and a quenching agent, and a method of use thereof, wherein the saponin is unheated or heated in the presence of absence of an acid. The specification discloses that modified saponins are synthesized by heating at 121 degrees in a solution that can contain an acid. The specification teaches that saponin derivatives made by said method are "significantly different from the original saponin" and can be used in a much broader range of derivative concentration for the hemolysis method (p. 4). The specification does not disclose the nature of the modification made by the heating of the saponin that is responsible for the increased stability. The specification does not disclose if one skilled in the art can utilize any possible temperature above room temperature to obtain the hemolysis reagent

comprising a heated saponin with the desired hemolytic characteristics with a reasonable expectation of results. Applicants point out that the saponin reagent kept at room temperature for up to 8 months loses its activity (p. 11). Hence, it is highly desirable obtain a stabilized saponin reagent. However, the specification shows one preparative method (heating at 121 degrees C for 30 min.) to obtain a product that is characterized as having as being more stable than the unheated product.

The prior at discloses that synthetic glycoside can be deacylated via acid catalyzed reflux to obtain the sugar and the aglycone (Segal (1978), p. 1591, right column). Shinohara (US 4,217,345) teaches that esterified soyasopogenal derivatives of soyasopogenal B can be de-esterified at a temperature from room temperature up to about 100 degrees C to obtain the alcoholic product (col. 5-6). Neither prior art document teaches that the heating process imparted any particular stabilization of the saponin.

It appears that the stabilization imparted by the heating procedure is limited to a temperature of about 121 degree C. Hence, one skilled in the art would be unable to pick a temperature and reaction conditions to provide a modified saponin and expect it to possess the same set of properties. If the heating method is not generally applicable to any possible temperature, then the desired stabilization of the saponin would be considered individually. This would be considered undue experimentation.

There is no reliable method that predicts which temperature/reaction conditions produce the stabilized saponin specie that is described in the specification. The prior art teaches the heating of various saponins but does not disclose that any particular stability was imparted to the modified saponin by the heating process. The specification does not teach how one of ordinary skill in the art could decide *a priori* which reaction conditions/temperatures will provide a saponin with the desired characteristics. The limited disclosure cannot be extrapolated by the skilled artisan to predict which reaction conditions/temperatures other than 121 degrees C will produce a stabilized saponin with the desired hemolytic activity. It would require one of ordinary skill in the art undue experimentation to determine what reaction conditions/temperatures other than 121 degrees C will produce a stabilized saponin

according to the directions of the instant disclosure. Thus, claims 1, 5, 6-8, 13 and 14 are not commensurate in scope with the enabling disclosure.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-3, 6, 7, 9-11, 13, 15-17 and 19 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Crews et al. ("Crews," (US 2002/009589; Reference A28 in the IDS filed 8/4/04).

Crews discloses a lysing agent and a quencher for the hemolysis of RBC prior to leukocyte analysis. The lytic agent comprises an acid and an active natural detergent. The acid can be a C-1 to C-3 carboxylic acid such as 2-chloro- and 2-fluoroacetic acids (section 0046, bridging sentence), which meets the limitation of a lytic reagent having a halogenated carboxylic acid, as in instant claims 17, 9, 13 and 19. The natural detergent is a saponin (section 0047), as in instant claims 1, 7, 13 and 19. The pH of the quenching agent is about 9.75, as in instant claims 13 and 19. Crewe further discloses that the saponin lytic agent can further comprise a non-ionic surfactant, *p*-nonylphenolpolyethoxylate, as in instant claims 2, 3, 10, 11, 16 and 17. Thus, Crews discloses a hemolysis reagent solution comprising a saponin, a halogenated acid, a non-ionic surfactant and a quenching agent wherein the acid is free of formic or acetic acids (instant claim 6).

The disclosure anticipates the method of instant method claim 13, 15-17 and 19 because Crews teaches that whole blood is contacted with a saponin and a halogenated acid to lyse the RBC. The lysing action is halted by the addition of a basic quenching agent having a pH of about 9.5. This pH values falls

within the range of meets the reagent system limitations for instant claim 19. The pH of the neutralized mixture is in the range of about 6.5 to about 7.2 (Ex. II, section 0078). The disclosed pH overlap the instantly claimed range of about 3 to about 6 (instant claim 13) because the metes and bounds of the term "about" is not specifically defined by the specification. Thus, the broadest reasonable interpretation of "about 6" includes the 0.5 pH unit that is included in the pH of "about 6.5" as disclosed by Crewe.

Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 6, 7, 9-13, and 15-19 rejected under 35 U.S.C. 103(a) as being unpatentable over Crews et al. ("Crews" (US 2002/009589; Reference A28 in the IDS filed 8/4/04), as applied to claims 1-3, 6, 7, 9-11, 13, 15-17 and 19, in further view of Malin et al. ("Malin"; (US 5,639,630).

The disclosure by Crews is discussed *supra.*

The disclosure by Crews does not teach that the nonionic surfactant is selected from the group consisting of an ethoxylated decylalcohol or an ethoxylated and propoylated linear (C8-C10) aliphatic alcohol or a combination thereof.

Malin is directed to a reagent and method for performing white blood cell differential counting and subpopulation analysis with fresh and aged RBC samples. The reagent of Malin comprises a nonionic polyethoxylate surfactant, an ionic surfactant and a chemical cross-linker. The surfactants are responsible for lysing the RBC (see claim 1). Malin discusses the different types of nonionic surfactants including the

two domain polyethoxylates which are the polyethoxylated alcohols, as in instant claims 4, 12 and 18, and the polyethoxylated phenols (col. 40, lines 56-67). The alcoholic type surfactant comprises hydrophobic domains such as long-chain branched or straight alcohols. The phenolic type comprises octyl- or nonyl-phenyl moieties (col. 41, lines 1-9). Thus, Malin demonstrates that polyethoxylated nonylpenyl and polyethoxylated long chain alcohol compounds being to the same class of non-ionic surfactants and are expected to have similar hemolytic abilities.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute a polyethoxylated long chain alcohol non-ionic surfactant for the polyethoxylated nonylphenol (referred to as *p*-nonylphenolpolyethoxylate by Crews) in the reagent employed by Crews for lysing RBC while preserving the leukocytes. The ordinary artisan would have been motivated to do so because the two surfactants are art-recognized equivalents, as taught by Malin. According to the MPEP 2144.06 (SUBSTITUTING EQUIVALENTS KNOWN FOR THE SAME PURPOSE): In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. In re Ruff, 256 F.2d 590, 118 USPQ 340 (CCPA 1958) (The mere fact that components are claimed as members of a Markush group cannot be relied upon to establish the equivalency of these components. However, an applicant's expressed recognition of an art-recognized or obvious equivalent may be used to refute an argument that such equivalency does not exist.); An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout, 675 F.2d 297, 213 USPQ 532 (CCPA 1982). In the instant case, Malin clearly shows that polyethoxylated long-chain alcohols and polyethoxylated nonlyphenols are recognized as belonging to the same class of nonionic surfactants and would be expected to have the same hemolytic effect on RBC.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Susan Hanley
Patent Examiner
1651

JEAN C. WITZ
PRIMARY EXAMINER